Further Mathematical Biology: Problem Sheet 5
Michaelmas Term 2020

Question 1.

The following equations describe the growth of a tumour that is radiated by an X-ray source,

$$\begin{aligned}
\frac{\partial C}{\partial t} &= D\frac{\partial^2 C}{\partial x^2} - kC \quad \text{for } |x| < R(t), && (1)\\
\frac{\partial C}{\partial x} &= 0 \quad \text{at } x = 0, && (2)\\
C(R(t), t) &= C_0, && (3)\\
\frac{\mathrm{d}R}{\mathrm{d}t} &= \int_0^{R(t)} (\alpha C - \beta)\mathrm{d}x, && (4)\\
R(0) &= R_0, && (5)
\end{aligned}$$

where k is the rate of nutrient uptake, α relates the tumour growth rate to the nutrient concentration, and β relates the strength of the X-ray source to the rate of tumour cell death.

(a) Using the substitutions

$$x = R_0\xi, \quad R(t) = R_0 r(\tau), \quad C(x,t) = C_0 c(\xi,\tau), \quad t = \frac{\tau}{\alpha C_0}, \tag{6}$$

and assuming that $\alpha C_0 R_0^2/D \ll 1$, show that the dimensionless system is

$$\begin{aligned}
0 &= \frac{\partial^2 c}{\partial \xi^2} - \mu c \quad \text{for } |\xi| < r(\tau), && (7)\\
\frac{\partial c}{\partial \xi} &= 0 \quad \text{at } \xi = 0, && (8)\\
c(r(\tau), \tau) &= 1, && (9)\\
\frac{\mathrm{d}r}{\mathrm{d}\tau} &= \int_0^{r(\tau)} (c - \gamma)\mathrm{d}\xi, && (10)\\
r(0) &= 1. && (11)
\end{aligned}$$

State expressions for the dimensionless parameters μ and γ.

(b) Show that the concentration of nutrient inside the tumour is given by

$$c(\xi,\tau) = \frac{\cosh(\sqrt{\mu}\,\xi)}{\cosh(\sqrt{\mu}\,r(\tau))}, \quad |\xi| < r(\tau). \tag{12}$$

(c) Hence show that the differential equation governing the size of the tumour is

$$\frac{\mathrm{d}r}{\mathrm{d}\tau} = \frac{1}{\sqrt{\mu}}\tanh\left(\sqrt{\mu} r(\tau)\right) - \gamma r(\tau) \tag{13}$$

(d) Find an expression for the minimum dose, β^*, in terms of the other dimensional parameters, that will completely destroy the tumour. Discuss what will happen to the tumour in the cases $\beta = 0$ and $0 < \beta < \beta^*$. [Hint: graph the two terms in the right-hand side of Equation (13) as a function of r.]

Question 2.

We will consider the following model for the growth of a spherically-symmetric tumour of volume V:

$$
\begin{aligned}
\frac{\partial C}{\partial t} &= \frac{D}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right) - \lambda \quad \text{for } 0 \le r < R(t); && (14)\\
\frac{\partial C}{\partial r} &= 0 \quad \text{at } r = 0; && (15)\\
C(R(t),t) &= C^*; && (16)\\
\frac{\mathrm{d}V}{\mathrm{d}t} &= 4\pi\int_0^{R(t)} P(C) r^2 \mathrm{d}r; && (17)\\
R(0) &= R_0. && (18)
\end{aligned}
$$

(a) Justify the model, taking care to describe the meaning of each term in the model equations.

(b) Nondimensionalise the system, scaling lengths with R_0, concentrations with C^*, P with a typical tumour proliferation rate P_0, and time with $1/P_0$. Assuming that $R_0^2 P_0/D \ll 1$, show that the model reduces (approximately) to

$$
\begin{aligned}
\frac{1}{\rho^2}\frac{\partial}{\partial \rho}\left(\rho^2\frac{\partial c}{\partial \rho}\right) &= \mu \quad \text{for } 0 \le \rho < s(\tau), && (19)\\
\frac{\partial c}{\partial \rho}(0,\tau) &= 0, && (20)\\
c(s(\tau),\tau) &= 1, && (21)\\
s^2\frac{\mathrm{d}s}{\mathrm{d}\tau} &= \int_0^{s(\tau)} p(c)\rho^2 \mathrm{d}\rho, && (22)\\
s(0) &= 1, && (23)
\end{aligned}
$$

where $s(\tau)$ is the dimensionless tumour radius, and μ is a dimensionless parameter that you should define.

(c) By solving Equations (19)–(23), show that when $p(c) = c$ the tumour radius, $s(\tau)$, satisfies the first-order ordinary differential equation

$$
\frac{\mathrm{d}s}{\mathrm{d}\tau} = \frac{s}{3}\left(1 - \frac{\mu s^2}{15}\right), \quad s(0) = 1. \qquad (24)
$$

(d) What are the steady states for the tumour radius?

(e) Show that the tumour-free steady state is unstable and comment on whether the nontrivial steady state is physically realistic.

Question 3.

Consider the following dimensionless model for the growth of a multicellular spheroid

$$\frac{\partial^2 c}{\partial \xi^2} = \mu \quad \text{for } -r(\tau) \leq \xi \leq r(\tau), \tag{25}$$

$$c(\xi, \tau) \equiv 1 \quad \text{for } \xi \geq r(\tau), \tag{26}$$

$$\frac{\partial c}{\partial \xi}(0, \tau) = 0, \tag{27}$$

$$c(r(\tau), \tau) = 1, \tag{28}$$

$$\frac{\mathrm{d}r(\tau)}{\mathrm{d}\tau} = \int_0^{r(\tau)} p(c)\mathrm{d}\xi, \tag{29}$$

$$r(0) = 1, \tag{30}$$

where the cells occupy $|\xi| \leq r(\tau)$, $c(\xi, \tau)$ is the nutrient concentration, μ is the rate at which it is taken up by the cells, and the cell proliferation rate, $p(c)$, is a function of the nutrient concentration.

(a) Suppose that the proliferation function p is given by $p(c) = c^2$. By solving Equations (25)–(28), show that the position, $r(\tau)$, of the outer radius of the spheroid is governed by the ordinary differential equation

$$\frac{\mathrm{d}r}{\mathrm{d}\tau} = r\left(1 - \frac{2}{3}\mu r^2 + \frac{2}{15}\mu^2 r^4\right). \tag{31}$$

(b) Find the steady states, and show that the only physically-relevant steady state is $r(\tau) \equiv 0$.

(c) By conducting a linear stability analysis of this trivial steady state deduce that it is unstable. What are the implications of these results for the growth of the spheroid in Equation (31)?

(d) Assuming that the given form for p is realistic for all positive nutrient concentrations, c, what would happen in the model in practice to make the solution break down?